REMARKS / ARGUMENTS

The Non-Final Office Action mailed May 15, 2007, was received and reviewed. Claims 1 through 34 are pending in the Application, and claims 1 through 15 are withdrawn from consideration as being directed to a non-elected invention. Claims 16 through 34 were rejected.

Applicants gratefully acknowledge the withdrawal of the prior rejection of claims 18-20, 24-26, and 31-34 under 35 U.S.C. § 101, and the withdrawal of the prior rejection of claims 21-26 under 35 U.S.C. § 103(a). The amendments provided above and remarks and arguments provided below address the new rejections, as set forth in the Non-Final Office Action mailed May 15, 2007.

Applicants respectfully request reconsideration of the Application by the Examiner in view of the amendments provided in response to the newly raised rejections, and in further view of following remarks and arguments.

CLAIM AMENDMENTS

Claims 1-3, 5, 6, 11, 12, 14-16, 18-21, and 24-26 are being amended as shown. In particular, claims 1-3, 11, 12, 16 and 18 have been amended by the insertion of the term "10 or more" following the phrase "a plurality of." Support for these amendments can be found on page 60, line 29, page 65, line 11 and page 67, line 1 of the specification, respectively. Claims 21 and 24 are being amended to define an intermediate number of expression vectors (claim 21) or cells or organisms (claim 24) between that of independent claims 16 and 18, respectively, and that of subsequent dependent claims 22 and 25, respectively. Support for these amendments can be found on page 65, line 11, and page 65, lines 1 and 6 of the specification, respectively. Additionally, claims 1-3, 5, 6, 11, 12, 14, 15, 18-20, and 24-26 are being amended to remove the phrase "non-human organism" and to uniformly recite "target cell cultures" wherever "cells," or "target cells" were referred to previously.

These amendment(s) should be entered into the record because they neither add new matter to the Application, nor raise any new issues that would require further search. Furthermore, these amendments place the claims in condition for allowance, or, alternatively, in better condition for appeal.

THE REJECTIONS

35 USC § 112, 2nd Paragraph

Claims 16-29 and 31-33 stand rejected under 35 USC § 112, 2nd paragraph, as allegedly being indefinite for failing to point out and distinctly claim the subject matter which the applicant regards as the invention. According to the Office Action of May 15, 2007, the term "chimeric RNA transcript" is allegedly indefinite. Applicants respectfully traverse this rejection and ask that the Examiner reconsider and withdraw this rejection in view of the following arguments.

As a first matter, Applicants respectfully note that regarding rejections under 35 U.S.C. § 112, second paragraph, The Manual of Patent Examining Procedure (MPEP) teaches the following.

Definiteness of Claim Language:

> "The essential inquiry pertaining to [the definiteness] requirement [of 35 U.S.C. § 112, second paragraph] is whether the claims set out and circumscribe a particular subject matter with **a reasonable degree of clarity and particularity**. Definiteness of claim language must be analyzed, not in a vacuum, but **in light of**:
> (A) **The content of the particular application disclosure**;
> (B) **The teachings of the prior art**; and
> (C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made."

MPEP 2173.02, 8th Ed., Rev. 5, Aug. 2006, p. 2100-211; emphasis added.

Breadth is Not Indefiniteness:

> "**Breadth of a claim is not to be equated with indefiniteness**. In re Miller, 441 F.2d 689, 169 USPQ 597 (CCPA 1971). If the scope of the subject matter embraced by the claims is clear, and if applicants have not otherwise indicated that they intend the invention to be of a scope different from that defined in the claims, then the claims comply with 35 U.S.C. 112, second paragraph."

MPEP 2173.04, 8th Ed., Rev. 5, Aug. 2006, p. 2100-213; emphasis added.

Importantly, the MPEP does not require that patent claims set out and circumscribe a particular subject matter with **absolute** clarity and particularity, but rather, with "**a reasonable degree** of clarity and particularity," such that the claims would be understood by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. Indeed, the United States Court of Appeals for the Federal Circuit (Federal Circuit) recently noted:

> The requirement to 'distinctly' claim means that **the claim must have a meaning discernible to one of ordinary skill in the art** when construed according to correct principles. … Only when a claim remains insolubly ambiguous without a discernible meaning after all reasonable attempts at construction must a court declare it indefinite.

Metabolite Labs., Inc. v. Lab. Corp. of Am. Holdings, 370 F.3d 1354, 1366, 71 USPQ2d 1081, 1089 (Fed. Cir. 2004); emphasis added.

Additionally, the Federal Circuit has made clear that "[t]he test for definiteness under 35 U.S.C. § 112, second paragraph is whether "those skilled in the art would understand what is claimed when the claim is read in light of the specification." *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1576, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986), emphasis added. (*See MPEP* Section 2173.02, 8th Ed., Rev. 5, Aug. 2006, p. 2100-212.) While critical limitations in the specification cannot be read into the claims, claim terminology must be read "in view" of the teachings of the specification. Furthermore, it is a well established tenant of patent law that claim terms are not to be viewed in vacuum. Established law asserts that where the specification defines a claim term such that an ordinarily skilled artisan would understand the meaning of the claim term, then the requirements of § 112, second paragraph are met.

Turning now to the specifics of the rejection under 35 U.S.C. § 112, second paragraph, the Office asserts that "neither the claims nor the specification define the term "chimeric RNA transcript" in a manner that would clearly inform one of skill in the art as to which polynucleotide sequences are **specifically** included and/or excluded by the claimed kits." (Office Action, p. 3, 2nd paragraph, emphasis added.)

In response, Applicant first note that the specification clearly defines "chimeric RNA transcript" to mean "an RNA transcript comprising a subject RNA operably linked to a universal target RNA to create a single RNA that does not naturally occur in nature" (*Specification*, p.16, ll. 28-30). Additionally, the specification defines "subject RNA" as "an RNA whose cellular concentration is to be altered, manipulated or reduced, or knocked down, by the action of an interfering RNA targeting the universal target RNA, but not the subject RNA" (*Specification*, p.16, ll. 25-27); and defines "universal target RNA," or UtRNA, as "a common RNA that is incorporated into a plurality of chimeric RNA transcripts, and serves to impart upon the chimeric RNA transcripts a susceptibility to degradation by RNA interference promoted by a "universal interfering RNA" targeting the universal target RNA" (*Specification*, p.17, ll. 5-9). The

specification further defines the term "operably linked," when used in the context of a chimeric RNA transcript, to mean "joined directly or indirectly such that the universal target RNA facilitates the reduction in concentration of at least the subject RNA when the chimeric RNA transcript is subjected to RNA interference induced by a universal interfering RNA" (*Specification*, p.17, ll. 2-4). Finally, the specification provides five drawings that depict the chimeric RNA transcripts of the present invention, and methods of using these chimeric RNA transcripts in accordance with the claimed invention.

Applicants respectfully assert that the skilled artisan, when presented with this collection of definitions, and the five drawings, would understand whether or not a chimeric RNA transcript in their possession would fall within the scope of the chimeric RNA transcripts of the claimed invention. Consequently, Applicants respectfully assert that the claim term "chimeric RNA," as used in the specification and the claims, would have a definite meaning to the skilled artisan.

Applicants confirm that the specification does not explicitly provide "which polynucleotide sequences are **specifically** included and/or excluded," because (a) the present invention was envisioned by the inventors to include essentially any polynucleotide sequences that had the appropriate structural and functional characteristics as specified in the definitions provided and (b) the claims were drafted to provide a scope sufficient to encompass that which the inventors perceived as their invention – in other words, the claims were drafted with specific terms, which were purposefully defined to encompass any polynucleotide sequences that had the appropriate structural and functional characteristics necessary to practice the full scope of the invention. Applicants concur that the term "chimeric RNA transcript," as defined in the specification encompasses a broad range of possible RNA molecules, however, Applicants respectfully remind the Examiner that "[b]readth of a claim is not to be equated with indefiniteness." In re Miller, 441 F.2d 689, 169 USPQ 597 (CCPA 1971).

In view of the above, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

35 USC § 112, 1st Paragraph – Written Description – New Rejection

Claims 16-29 and 31-33 stand rejected under 35 USC § 112, as allegedly "failing to comply with the written description requirement," because the claims allegedly "contain subject

matter which was not described in the specification is such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention."

As a first matter, compliance with the "written description requirement" is a question of fact. For this reason, the MPEP § 2163.04 notes: "The examiner has the initial burden of presenting **by a preponderance of evidence** why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims. *Wertheim*, 541 F.2d at 263, 191 USPQ at 97." (MPEP, 8th Ed., Rev. 5, August 2006, pp. 2100-180; emphasis added). MPEP § 2163.04 further instructs:

> In rejecting a claim, the examiner must set forth **express findings of fact** which support the lack of written description conclusion .... **A general allegation of "unpredictability in the art" is not a sufficient reason to support a rejection for lack of adequate written description**.

(MPEP, 8th Ed., Rev. 5, August 2006, pp. 2100-187; emphasis added).

Applicants respectfully assert that, in the present case, the Office Action fails to provide any **evidence or express findings of fact** as to why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims.

As a second matter, the United States Court of Appeals for the Federal Circuit has made clear the following three points in *Capon v. Eshhar* (418 F.3d 1349, Fed. Cir. 2005). First, "[t]he descriptive text needed to meet [the written description requirement] varies with the nature and scope of the invention at issue, and with the scientific and technologic knowledge already in existence." *Id* at 1357. Second, "[t]he written description requirement may be satisfied "if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure." *Id* at 1357. Third, "[i]n the patent context, the written description **must** be applied in the context of the particular invention and the state of the knowledge." *Id* at 1358.

Additionally, the United States Patent and Trademark Office (PTO) has issued guidelines for the examination of patent applications under the 35 USC § 112, first paragraph, written description requirement. These guidelines state that the written description requirement of 35 USC § 112, first paragraph, can be met by:

> show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ... i.e., complete or partial structure, other

> physical and/or chemical properties, **functional characteristics when coupled with a known or disclosed correlation between function and structure**, or some combination of such characteristics.

Guidelines for Examination of Patent Applications under 35 USC § 112, first paragraph, "Written Description" Requirement, 66 Fed. Reg. 1099, 1106 (Jan. 5, 2001) (emphasis added).

Applicants respectfully note that the nexus of the instant invention was the realization that the expression of any number of recombinant proteins from chimeric RNA transcripts could be disrupted by RNA interference induced by the action of a single, pre-selected, "universal interfering RNA" (i.e., an siRNA or shRNA), if that universal interfering RNA targeted a commonly shared sequence incorporated into the plurality of chimeric RNA transcripts. Applicants further note that the "fundamental elements" of the invention, include (a) the shared, common target sequence (a "universal target sequence" that can be located essentially anywhere in the recombinant transcript), and (b) the corresponding universal interfering RNA that acts by targeting the universal target sequence and inducing RNA interference – and such elements were already available to the skilled artisan at the time the invention was made.

Furthermore, Applicants respectfully remind the Examiner that the pending claims are drawn towards kits for practicing a novel method – and are NOT drawn towards novel compositions of matter such as novel genes, novel segments of DNA, or even novel siRNAs or shRNAs. Consequently, holding the instant specification to the standard of written description required for novel genes, novel segments of DNA, or even novel siRNAs or shRNAs would be inappropriate. As the specification makes amply clear, and as the pending claims suggest, known nucleic acids can be used in the claimed kits and methods of the invention, both in the context of universal target RNAs and the interfering siRNAs and shRNAs that target them. In other words, the concept of "RNA interference using a universal target" does not require the development of new nucleic acid components with novel activities, instead, it can encompass the use of new combinations of previously known components. (See below for an example.)

State of the Art:

Applicants respectfully assert that the "written description rejection," as presented in the Office Action, essentially ignores the state of knowledge in the relevant arts at the time the instant Application was filed. Additionally, the Office Action fails to recognize that the written

description requirement may be satisfied "if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure." *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1332 (Fed. Cir. 2003); as recited in *Capon v. Eshhar*, 418 F.3d 1349 (Fed. Cir. August 12, 2005).

Applicants note that at the time the instant Application was filed, skilled artisans were well aware that RNA interference was induced by siRNAs and shRNAs with particular, known structures. Further, the instant Application teaches in detail (in Section 7, pages 39 - 41) the general structures of siRNAs and shRNAs required to induce RNA interference, and the methods by which they can be created and introduced into cells, tissues or organisms. The specification also provides references to critical and informative publications providing additional teachings as well as clear documentation as to what was within the purview of the skilled artisan at the time the instant Application was filed.

In addition to these teachings, as indicated above, the prior art provides all the necessary elements to create embodiments of the instant invention, and further provides sufficient proof of concept to demonstrate that the instant invention is adequately described. Specifically, the prior art contains descriptions of examples of chimeric RNA transcripts comprising a "subject RNA" operably linked to a "target RNA," which do not naturally occur in nature, and which can be targeted for degradation by RNA interference with an siRNA or shRNA that corresponds in sequence to at least a portion of the operably linked target RNA, and not the subject RNA. Thus, in essence, the prior art puts skilled artisans in possession of all of the necessary elements of the invention, however, the prior art fails to teach that the same siRNA or shRNA can be used to target a plurality of chimeric RNA transcripts, each bearing a different subject RNA operably linked to a shared, "universal," target RNA.

As evidence in support of this assertion – that the necessary elements required to create an embodiment of the instant invention were available in the art prior to the filing of the instant Application – Applicants first note that the instant Application states "For example, the [universal target RNA] can encode enhanced green fluorescent protein, or any other variety of fluorescent protein." (Specification, page 38, lines 10-11.) Applicants next note that in an article published on August 14, 2001, Caplen *et al.*, taught that enhanced green fluorescent protein (EGFP) recombinantly-expressed in mouse embryonic fibroblasts can be effectively knocked down using chemically-synthesized siRNAs corresponding to the target region

comprising nucleotides 122-141 of the EGFP coding sequence (GCAAGCUGACCCUGAAGUUC) (Caplen *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* 98:9742-9747 (2001); provided to the Office as *Exhibit B* with the Amendment Under 37 C.F.R. § 1.116, filed May 19, 2006). (This same target sequence was also effectively targeted in HeLa cells recombinantly-expressing EGFP by Donzé & Picard, using enzymatically-synthesized siRNA of the same sequence, according their May 15, 2002 publication (Donzé & Picard. *Nucleic Acids Res*. 30:e46 (2002); provided to the Office as *Exhibit C* with the Amendment Under 37 C.F.R. § 1.116, filed May 19, 2006).

As further evidence that these "prior art elements" can be used to practice the methods of the instant invention, Applicants note these same prior art elements reappear in an article describing a "new and universal transgene silencing method based on RNA interference," which was published 9 months after the filing of the instant Application. (See Mangeot *et al.*, *Nucleic Acids Res*. 32:e102 (2004); provided to the Office in the IDS filed March 3, 2004). In demonstrating the effectiveness of this method for silencing transgene expression, Mangeot *et al.*, employ an shRNA that targets the same 20 nucleotides of the EGFP coding sequence targeted by Caplen *et al.* and Donzé & Picard. However, in this embodiment of a "universal transgene silencing method," the EGFP target sequence is not present within the context of a transcript that only encodes full-length EGFP (as it was in the studies of Caplen *et al.* and Donzé & Picard), but rather, it is contained within the context of either a bicistronic transcript encoding human thioredoxin and full-length EGFP, or, alternatively, it is embedded, as part of a 25 nucleotide fragment of the EGFP coding sequence, within the 3'-untranslated region of a chimeric RNA transcript encoding human thioredoxin.

In view of these facts, Applicants assert that it is amply clear that the knowledge of the art provides a disclosed function [induction of RNA interference], which has been sufficiently correlated to a particular, known structure [specific target RNAs, and the siRNAs and shRNAs act on that target to induce RNA interference]. Hence, the teachings of the art satisfy the written description requirement, with respect to the elements required to practice the claimed invention.

Applicants further note that the Office Action presents no factual evidence indicating why a person skilled in the art would not recognize in the Applicants' disclosure a description of the invention defined by the claims, in view of the knowledge in the art at the time the application was filed.

In summary, it is submitted that the descriptions provided in the specification constitute sufficiently detailed, relevant identifying characteristics of the claimed subject matter consistent with *Enzo*, and the USPTO's own "Written Description Guidelines." It is also submitted that the instant Office Action has failed to establish why one of ordinary skill in the art, provided with the descriptions of the specification, combined with the teachings of the prior art, would be unable to recognize invention defined by the claims. Finally, as stated by the Federal Circuit in *Capon v. Eshhar*:

> "The "written description" requirement must be applied in the context of the particular invention and the state of the knowledge. … When the prior art includes nucleotide information, precedent does not set a per se rule that the information must be determined afresh. … As each field evolves, the balance evolves between what is known and what is added by each inventive contribution. … It must be borne in mind that, while it is necessary that an applicant for a patent give to the public a complete and adequate disclosure in return for the patent grant, the certainty required of the disclosure is not greater than that which is reasonable, having due regard to the subject matter involved."

Capon v. Eshhar, 418 F.3d 1349 (Fed. Cir. August 12, 2005); at 1358 & 1360.

Accordingly, Applicants assert that claims 16-29 and 31-34 are based upon a specification that provides adequate written description of the claimed invention, and request that written description rejection under 35 USC **§** 112, first paragraph, be withdrawn.

35 USC § 101

Claims 16-34 stand rejected under 35 USC § 101, because the claimed invention allegedly lacks either a credible, specific and substantial utility or a well established utility. Applicants respectfully disagree and traverse the rejection. Applicants ask that the Examiner reconsider and withdraw the rejection in light of the following arguments.

According to the Office Action, the claimed invention lacks utility because the specification identifies the use of the claimed kits for 1) "investigating gene function" and 2) "treating disease," and these two asserted utilities do not meet the standard for a specific and substantial utility. Applicants respectfully submit that in framing the rejection of the claimed invention on the basis of 35 USC § 101, the Examiner has selected two asserted utilities that serve as "easy targets" for the rejection, while simply ignoring other asserted utilities for the claimed invention.

MPEP § 2107.02 instructs:

> It is common and sensible for an applicant to identify several specific utilities for an invention, particularly where the invention is a product (e.g., a machine, an article of manufacture or a composition of matter). However, regardless of the category of invention that is claimed (e.g., product or process), an applicant need only make one credible assertion of specific utility for the claimed invention to satisfy 35 U.S.C. 101 and 35 U.S.C. 112.

MPEP § 2107.02, 8th Ed., Rev. 5, Aug. 2006, p. 2100-28.

Applicants note that the specification provides many asserted utilities for the kits of the claimed invention, and the underlying methods that the kits facilitate. In particular, the specification asserts that, at its most basic level, the claimed invention provides "novel methods for altering levels of expression of a plurality of gene products using RNA interference (RNAi) induced by a "Universal interfering RNA" (UiRNA) directed towards a commonly-shared "Universal target RNA" (UtRNA)." Specification, p. 7, ll. 15-18. For instance, the specification teaches:

> Advantageously, the methods of the present invention provide a means for targeting a plurality of recombinantly expressed gene products for RNA interference, by providing a plurality of expression vectors that direct the expression of a plurality of chimeric RNA transcripts, each comprising a different, unique subject RNA preferably encoding a particular gene product, and a common UtRNA. These expression vectors are then introduced into target cells or organisms, which are capable of transcribing the chimeric RNA transcripts and translating the encoded gene products, thereby creating a plurality of transfected target cells or organisms, each collection of target cells or organism transfected with the same expression vector expressing the same chimeric RNA transcript and encoded gene product. … A UiRNA that is capable of inducing RNAi by targeting the common UtRNA shared by all expression vectors and chimeric RNA transcripts, in all transfected target cells or organisms can then be introduced into these transfected target cells or organisms to simultaneously reduce expression of all recombinantly expressed gene products.

Specification, p. 9, ll. 4-20.

Applicants respectfully assert that this passage of the specification provide a credible assertion of specific and substantial utility for the claimed invention that clearly satisfies 35 U.S.C. § 101 and 35 U.S.C. § 112. Support for this assertion and its credibility is found in the successful application of the general concepts of the methods of the instant invention as reported in the post-filing art reported by Mangeot and coworkers (Mangeot *et al.* A universal transgene

silencing method based on RNA interference. *Nucleic Acids Res*. 32(12):e102 (2004)) which was provided to the Office in the Information Disclosure Statement filed on March 3, 2005.

Additionally, the specification teaches:

> The methods of the present invention, when utilized in organisms or cells exhibiting transitive RNAi, provide a method of reducing the expression of a plurality of endogenous genes, using a UiRNA that is targeted to a UtRNA, when a nucleotide sequence encoding the endogenous gene, or a homologue thereof, is included along with a UtRNA in a single chimeric RNA transcript. Consequently, in organisms or cells that either naturally exhibit transitive RNAi, or are made to carry out transitive RNAi, the methods of the present invention provide a method for treating disease that involves reducing the cellular concentration of gene products encoded by endogenous RNA transcripts by first targeting a chimeric RNA transcript bearing a UtRNA and encoding a gene product whose endogenous expression is desired to be reduced, using UiRNA-induced RNAi to initially reduce the expression of the recombinantly expressed gene product, and allowing secondary siRNAs generated during that process to transit and cause the RNAi-mediated degradation of endogenous transcripts encoding the target gene product, and homologues thereof.

Specification, page 18, lines 6 through 19.

Hence, the specification asserts utility for the claimed invention specifically in organisms that exhibit transitive RNAi.

Applicants respectfully note that similar such utilities were identified by the Office in rejecting claims 16-20 and 27-34 under 35 U.S.C. § 103(a), for allegedly being unpatentable over the cited references. Indeed, the Office has suggested that there is a motivation to combine the references (and thereby arrive at the claimed invention of claims 16-20 and 27-34) in order "to study transitive RNAi in *C. elegans* and other organisms including *Drosophila* and plants," and "define and elucidate transitive RNAi and/or amplification mechanisms in a variety of organisms" (Office Action, p. 30). The Office further asserts that the skilled artisan's motivation would come from the desire to understand the "importance of the [amplification] effect and possible systemic spread of RNAi in some organisms," to "define these mechanisms and more clearly understand the role [they] play in naturally occurring RNAi, as part of viral defense, for example in plants and/or higher eukaryotes," and, further, to "define the particular molecular requirements of transitive RNAi in any given organism" (Office Action, pp. 30-31).

Applicants submit that regardless of whether or not the rejection of claims 16-20 and 27-34 under 35 U.S.C. § 103(a) is proper, the Office has identified a set of real-world uses for the

kits of the claimed invention that are fully congruent with the utility asserted by Applicants at page 18, lines 6 through 19 of the specification.

In view of the above, Applicants assert that the claimed invention has credible, specific and substantial utility. Therefore, Applicants ask that the rejection of claims 16-34 under 35 USC § 101, be withdrawn.

35 USC § 112, 1st Paragraph – Written Description for Lack of Utility

Claims 16-34 stand rejected under 35 U.S.C. § 112, first paragraph, because the claimed invention is allegedly not supported by either a credible, specific and substantial asserted utility or a well established utility, so one skilled in the art would allegedly not know how to used the claimed invention.

As indicated above, the claimed invention is indeed supported by a credible, specific and substantial asserted utility, therefore this rejection under 35 U.S.C. § 112, first paragraph is moot.

35 USC § 112, 1st Paragraph – Enablement

Claims 18-34 stand rejected under 35 U.S.C. § 112, first paragraph, because the claimed invention is allegedly not supported by an enabling disclosure. Specifically, the Office Action (on page 19) asserts that "[e]nabling support does not exist for making and using the full scope of non-human organisms embraced by the claims."

As a first matter, claims 21-23 and 27-30, do not embrace non-human organisms. Rather, they read upon kits comprising a plurality of expression vectors. Consequently, the enablement rejection, as presented on pages 17-24 of the Office Action, does not apply to these claims. Therefore, Applicants respectfully request that the rejection of claims 21-23 and 27-30 under 35 U.S.C. § 112, first paragraph, for lack of enablement, be withdrawn.

In response to the rejection of claims 18-20, 24-26, 31 and 32, under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement, Applicants have amended the claims so that they no longer embrace non-human organisms, thereby obviating the rejection.

Applicants make these amendments without prejudice, and expressly reserve the right to pursue the deleted subject matter in a continuing application.

In view of the amendments provided, which have eliminated non-human organisms from the claimed subject matter, applicants respectfully request that the rejection of claims 18-20, 24-26, 31 and 32, under 35 U.S.C. § 112, first paragraph, for lack of enablement, be withdrawn.

35 USC § 103(a) – Obviousness

Claims 16-34 stand rejected under 35 U.S.C. § 103(a), for allegedly being unpatentable over Sijen *et al.* (2001) *Cell* 107:465-476; Pal-Bhadra *et al.* (1998) *Cell* 99:35-46; Voinnet *et al.* (1998) *Cell* 95:177-187; Fire *et al.* (1990) *Gene* 93:189-198; Kennerdell *et al.* (1998) *Cell* 95:1017-1026; and Elbashir *et al.* (2001) *Nature* 411:494-498. Applicants have amended the claims in response to this allegation and request reconsideration and withdrawal of this rejection in view of the following.

The section of the Office Action of May 15, 2007 addressing the withdrawal of the prior rejection of claims 21-26 under 35 U.S.C. § 103(a) concludes: "while the instant references taught and/or suggested the study of transitive RNAi in mammalian and non-mammalian organisms using artificial gene constructs and siRNA, **the combination of references does not explicitly or implicitly teach or suggest using multiple, i.e., 10 or more, such constructs** in any transitive RNA study." (Office Action at page 25, lines 4-7, emphasis added). Applicants respectfully note that "[t]he teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure." In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). MPEP § 2143, 8th Ed., Rev. 5, Aug. 2006, p. 2100-126.

In response to the Office's conclusion and the Federal Circuit's explicit teaching in In re Vaeck, Applicants have amended claim 16 to define a "plurality of expression vectors" as "10 or more expression vectors," and have amended claim 18 to define a "plurality of target cells or non-human organisms" as "10 or more target cells or non-human organisms." Concordantly, Applicants have amended claims 21 and 24 to respectively recite kits comprising appropriate intermediate numbers of expression vectors, or target cells or non-human organisms, in agreement with quantities specifically described in the specification.

Applicants believe that these amendment to claims 16, 18, 21 and 24 result in claims 16-34 meeting the requirements of 35 U.S.C. § 103(a), in view of Sijen *et al.* (2001) *Cell* 107:465-476; Pal-Bhadra *et al.* (1998) *Cell* 99:35-46; Voinnet *et al.* (1998) *Cell* 95:177-187; Fire *et al.*

(1990) *Gene* 93:189-198; Kennerdell *et al*. (1998) *Cell* 95:1017-1026; and Elbashir *et al*. (2001) *Nature* 411:494-498, since, as suggested by the Office, "**the combination of references does not explicitly or implicitly teach or suggest using multiple, i.e., 10 or more, such constructs.**" Consequently, Applicants respectfully request the withdrawal of the rejection of claims 16-34 under 35 U.S.C. § 103(a).

CONCLUSIONS

Claims 16 through 34 are believed to be in condition for allowance, and an early notice thereof is respectfully solicited. Should the Examiner determine that additional issues remain which might be resolved by a telephone conference, he is respectfully invited to contact the undersigned via his direct office line at 801-883-3463.

Additionally, should either claim 16 or 18, or both, be found to be allowable, Applicant respectfully requests rejoinder and examination of withdrawn process (method) claims (i.e., claims 1-15), in accordance with the provisions of MPEP § 821.04.

A petition for a two month extension of time for the filing of this response is being filed concurrently herewith. Provisions for the payment of the necessary fee have been made in the petition. Therefore, it is believed that no other extension of time, or any additional fees are due with this response. If this is incorrect, an extension of time as deemed necessary is hereby requested, and the Commissioner is hereby authorized to charge any appropriate fees, or credit any over payment, to Deposit Account no. **50-1627**.

Respectfully submitted,

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October 15, 2007

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